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FISKE FUND PRIZE DISSERTATION. No. XLII.

THE ETIOLOGY AND DIAGNOSIS
OF
EPIDEMIC
CEREBRO-SPINAL MENINGITIS

MOTTO:
"Keep Watch."

BY
ARCHIBALD WILLIAM TAYLOR, M.D.
NEW YORK, N. Y.

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THE Trustees of the Fiske Fund, at the annual meeting of the Rhode Island Medical Society, held at Providence, May 31, 1906, announced that they had awarded a premium of two hundred and fifty dollars to an essay on "The Etiology and Diagnosis of Epidemic Cerebro-Spinal Meningitis," bearing the motto:

"Keep Watch."

The author was found to be ARCHIBALD WILLIAM TAVES, M. D., of New York, N. Y.

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19249

THE ETIOLOGY AND DIAGNOSIS OF EPIDEMIC CEREBRO-SPINAL MENINGITIS.

For several hundred years there have been more or less extensive epidemics in Europe, which, viewed from our present knowledge, were probably epidemics of cerebro-spinal meningitis. But it remained for Vieusseaux at Geneva in 1805 to recognize the disease. Hirsch,¹ in an elaborate history of the disease which has been extensively quoted, divides the epidemic into four periods. The first ranged from 1805 to 1830. The outbreaks in Europe during this period differed from those in the United States by not being very widespread. In this country the New England States were particularly involved, and the States lying to the border of the Mississippi, and as far north as Canada. The second period, from 1837 to 1850, involved Western Europe, but France especially, and touched at Algiers, Sicily, and even Denmark and Iceland. During this period a widespread epidemic occurred in this country among the Western and Southern States. The third period, from 1854 to 1874, affected mainly Sweden, Germany and parts of Russia. In this country the disease spread widely during the civil war, and covered a large area. During the

fourth period, from 1876 to the present time, there have been no extensive epidemics in Europe, and none in this country except one during the last decade, which has selected mainly the Northern and Eastern States. During the past few years there have been a few thousand cases in New York City alone.

The disease occurs in unusual waves, distributed irregularly, and with a peculiar commencement and cessation of activity. It spreads at times by means of no well-defined channels, breaking out at apparently disconnected places. There is no regular curve of ascent, maximum and decline, and its behavior is spasmodic and erratic. Very large geographical sections do not ever seem to be extensively involved. An epidemic generally remains somewhat localized, where it stays for a variable length of time; and then it disappears, or recurs during successive seasons. There is no continuous extension; comparatively few in a community are attacked.

During the first half year of 1905 I had the opportunity of seeing 105 consecutive cases at Gouverneur Hospital in New York City, and have since studied the notes, records and charts made at the time. In this paper I shall refer to these cases as the "Gouverneur series" or the "Gouverneur cases."

Race and Sex: The statement that there seems to be no special racial disposition to the disease is borne

out by reading the geographical history of epidemic cerebro-spinal meningitis. The sexes are about equally liable to it, as far as can be gleaned from the literature of the subject. Of 365 cases collected by Billings,² in the recent epidemic in New York, 56 per cent. were in males.

Age: Hirsch collected statistics in 1267 fatal cases, and found that 71 per cent. were under fifteen years, 26 per cent. were between fifteen and forty years, and only three per cent. were over forty. The following table is from the Gouverneur series :

1 year or younger,	9 per cent. ; youngest, four months.
1 to 5 years,	38 per cent. ;
5 to 10 years,	23 per cent. ;
10 to 15 years,	21 per cent. ;
15 to 20 years,	6 per cent. ;
20 to 25 years,	3 per cent. ; oldest, 25 yrs.

Although a large proportion of the cases are generally between the ages of one and fifteen, still some epidemics have confined themselves to adults in early middle-life, as, for instance, the Italian epidemic between 1840 and 1845, and the one studied by Ames³ in Montgomery, Alabama. The epidemics in camp and garrison life are also another instance of this.

There seems to be some difference of opinion as to the occurrence of the disease under one year. Coun-

cilman⁴ believes it is exceedingly rare under that age. Undoubtedly before the discovery of the meningococcus, and the recognition of the facility with which lumbar punctures could be made and the diagnostic value of the fluid, a large number of deaths under one year have been erroneously attributed to epidemic cerebro-spinal meningitis. But, on the other hand, its prevalence under one year appears to be more common than is generally supposed. Thus, in the figures collected by Billings already referred to, out of 424 cases reported as epidemic cerebro-spinal meningitis 50 were deducted as not being genuine cases. Of the remaining 365 apparently true cases, 60 cases, or sixteen per cent. were under one year. In our own series nine per cent. were one year or younger.

Predisposition and Immunity: The question of predisposition or susceptibility is a very interesting one. There seems to be practically no racial predisposition. Concerning personal susceptibility, it is a well-known fact that comparatively few in a community are attacked during an epidemic; from this it would seem that personal susceptibility is uncommon, or, conversely that personal immunity is common. The fact that few in a community are attacked, however, does not appear to be an argument in favor of personal immunity, but rather one tending to prove that, comparatively, the disease is not readily communicable. It is well-known that several cases may

occur in the same house, a large number of cases in a small district, and often a large proportion of the occupants of a jail, camp, or barracks. The way in which a particular regiment has sometimes been decimated by it, speaks against personal immunity being very general or a very important factor in the matter.

Can immunity be acquired by a previous attack? This is a question which is difficult to settle. That one attack does not always confer immunity seems to be beyond any doubt. North,⁵ in 1811, mentions a case in which the second attack followed the first by over two years; and another in which an interval of nine months elapsed. Several instances of a second attack are mentioned in the literature of the subject, and yet few in proportion to the number of first attacks. This fact has led Councilman to believe that a relatively high degree of immunity must be conferred by a single attack. We undoubtedly need more light on the subject, for, in the first place, owing to the nature of the disease, it is not always easy to differentiate a subsequent attack from a relapse. The disease is irregular in its course, and characterized by exacerbations and relapses. A relapse may occur after the patient has been walking about in the ward, apparently well. It appears plausible that the meningococci may remain latent in the cerebro-spinal fluid for a variable length of time, and then take on renewed activity and virulence. Then again, the mortality is high and the prospect is not very great of a patient becoming ex-

posed for a second time to the infection. The disease also flits about, and after leaving a locality may never return again, or, at all events, not for a number of years; and, even should it return, its communicability does not appear to be very great. In the Gouverneur records there is one case of an undoubted second attack after an interval of five and a half months. In this connection it would be of interest to know for what length of time after an attack of epidemic cerebro-spinal meningitis the blood-serum possesses agglutinating properties against the meningococcus.

Communicability: The communicability of the disease does not appear to be very great. It is not contagious in the sense that the exanthemata are contagious. Its infectivity has been compared to about that of croupous pneumonia. House epidemics have occurred, but not in the sense that tuberculosis is a house disease; in epidemic cerebro-spinal meningitis the cases have occurred at or about the same time, and the meningococcus does not show a disposition to linger there and infect future occupants as in the case of tubercle bacillus. Osler⁶ mentions five cases occurring in a house within six weeks, and Gifford⁷ five cases in a family one after another within a week. Bolduan and Goodwin,⁸ in an elaborate article on the recent epidemic in New York, tabulate 58 instances in which two or more cases occurred to a house. In

the Gouverneur series nine instances were recorded in which there were two or more cases to a family. On the other hand members of a family, living in the same house or even sleeping in the same bed, often escape. Doctors, nurses and attendants are rarely stricken. Draper⁹ mentions a case, however, in which a former interne of Bellevue Hospital attended a patient with epidemic cerebro-spinal meningitis, and then developed the disease himself one week later. But direct propagation in this way appears to be rather uncommon.

In what manner, then, or by what means, is the disease communicated from one person to another? By what channel or channels does the meningococcus escape from the cerebral cavity and spinal canal to the exterior? What are the avenues of entrance, and do they remain infected during the course of the disease? These are questions which cannot be answered positively at the present time; but it is very suggestive that meningococci are found in the nasal secretions of about half the patients early in the disease. At a meeting of the American Public Association in Boston in September, 1905, Drs. Park and Bolduan¹⁰ stated that of 1500 cases, in the recent epidemic in New York, 200 had been in direct contact with other patients, and that many of these latter showed evidence of infection from still others. Considering the presence of the meningococci in the nasal secretion early in the disease, the conclusion was drawn that

the organism was spread by the nasal and buccal discharges of the sick and those in immediate contact with them. That part of the nasal mucous membrane is in close proximity to the meninges, and in this situation the numerous short olfactory nerves perforate the cribriform plate of the ethmoid and ramify in the soft tissues of the nares. The channels of infection may, of course, be by means of the lymphatics, the blood, or directly.

Is cerebro-spinal meningitis of the epidemic type invariably caused by the meningococcus? Our present data point to the negative. Marchal,¹¹ in an analysis of 418 epidemic cases, gives the meningococcus as the causative factor in over 73 per cent. of the cases; the pneumococcus in over 16 per cent., and other organisms in the remaining 10 per cent. And in 95 sporadic cases, the meningococcus was the causative factor in 50.5 per cent.; the pneumococcus in 42.1 per cent., and other organisms in 7.4 per cent. Other investigators have found the meningococcus rather more frequently in the epidemic cases. Bolduan and Goodwin say "it must always be remembered that cases of pneumococcus and of streptococcus meningitis are fairly common, and they will naturally occur also during an epidemic of meningococcic meningitis."

The specificity of epidemic cerebro-spinal meningitis is challenged by the preceding figures. Are we then to regard the epidemic form of cerebro-spinal

meningitis as an infective disease that may be caused by several different organisms? Is there a clinical identity without a pathological identity? Our present information does not permit these questions to be answered positively at the present time. But epidemic meningococcic meningitis appears in some cases to differ clinically from the primary pneumococcic form — and it is possible that in the future we shall be able to separate the primary forms clinically as well as pathologically into meningococcic cerebro-spinal meningitis and pneumococcic cerebro-spinal meningitis. It is probable when statistics are fully completed upon the recent epidemic in the Eastern States, that the meningococcus will be found associated with a greater percentage of the primary cases than has hitherto been found. In the Gouverneur series no other organism was found in the spinal fluid obtained; but unfortunately cultures were not made in every instance. Then, again, epidemic cerebro-spinal meningitis acts like a specific disease. It is also possible that in some of the cases where other organisms have been found that the meningococcus has been the actual precursor, but owing to its feeble vitality has disappeared under the influence of a secondary and more virulent infection by some other organism. Osler,¹² in his Cavendish Lecture of June 16, 1899, recognizes two forms of primary cerebro-spinal meningitis, the meningococcic and the pneumococcic; the former is subdivided into epidemic and sporadic types. He also

states that mixed infection is not uncommon; but believes that these invaders are in all probability secondary; the most common being the pneumococcus. Elsner¹³ also refers to mixed infection not being uncommon. There is an epidemic form of croupous pneumonia, and it is possible that primary pneumococcic meningitis may assume an epidemic type. In Councilman's series the pneumococcus was responsible for ten cases. It was primary in two cases, and secondary to some other lesion in eight. He further states that extensive epidemics have been reported as caused by the pneumococcus. Still, the question of specificity must be left *sub judice* at the present time. Suffice it to say that a large proportion of the cases of epidemic cerebro-spinal meningitis are associated with the meningococcus of Weichselbaum.

Other Factors: The influence of *heat* and *cold*, and *moisture*, are probably not very great, for, although the majority of the epidemics have occurred during the winter and spring months, still some have occurred during the warm weather. Cold weather in all probability exerts its influence by preventing proper ventilation and sanitation in houses. *Soil* and *situation* do not appear to play an important role; there is no unanimity of opinion in this respect. Country places have generally suffered more than cities, but during 1904-1905 an extensive epidemic occurred in New York City. Randolph¹⁴ considers that hygienic condi-

tions do not play a very important role, and Upham¹⁵ also says that the cases are distributed among all classes and grades of society. Epidemics of the disease in jails, camps and barracks have been referred to. In the late epidemic in New York City the sections mainly involved were the densely populated lower East-side, the crowded lower West-side, and that neighborhood centered about East 110th street known as "Little Italy." Gouverneur Hospital drew its patients from one of the most unsanitary neighborhoods in the city—one of over-crowded, badly ventilated tenements. There was practically no personal cleanliness whatsoever in a large number of the cases admitted.

Over-exertion has seemed to render recruits more liable to the disease than seasoned soldiers. A history of *traumatism* to the skull is only rarely obtained, and can play only a casual role, if any. In the Gouverneur series a history of trauma to the skull preceding the development of the disease was obtained in only five cases, and the onset after this varied from two days to two weeks. In the case of Max B., it seemed like a typical case of traumatic cerebral hemorrhage until the meningococcus was obtained by lumbar puncture. It is conceivable that, in this instance, the traumatism may have disarranged sufficiently the mucous membrane in the neighborhood of the cribriform plate to permit the entrance of the

organism. *Insect bites* were present in only a small proportion of the Gouverneur cases. If infection can take place in this manner it must be of rare occurrence as the meningococcus does not appear to be either usually or constantly present in the blood of epidemic cerebro-spinal meningitis cases, and when present they are probably in small numbers. Elsner¹⁶ was able to detect them in only ten out of forty-one cases. I have not been able to find an instance of a positive experiment with fleas, bedbugs, or other insects or vermin.

Relations to Other Diseases: Coryza and pharyngitis have preceded the onset of the meningitis in a small proportion of the cases. In this connection it is interesting to note that Kiefer,¹⁷ while working with a culture of meningococci, was seized with a violent coryza, and then was successful in isolating the meningococcus from his nasal secretion. A large proportion of the cases of epidemic cerebro-spinal meningitis, however, are suddenly stricken while in apparent good health. In the Gouverneur series over 80 per cent. were in the enjoyment of perfect health when attacked, and there seemed to be no special pathological condition associated with the remainder.

Relation to Pneumonia: Numerous monographs have been written, partly, if not wholly, upon the

relation of epidemic cerebro-spinal meningitis to croupous pneumonia. Thus, it has been stated that the seasonal relations are the same, that they often prevail together, that both are characterized by an abrupt onset, a leucocytosis, and the appearance of herpes, that the degree of infectivity is about the same, that one sometimes becomes a complication of the other, that the characteristics of the exudates are almost identical, and that sporadic cases in both diseases seem to be connecting links between epidemics. Leichtenstern,¹⁸ on the other hand, points out that pneumonia is a widely disseminated disease, no land being immune, whereas epidemic cerebro-spinal meningitis is comparatively rare, and in some countries unknown; that the susceptibility due to age is different in the two diseases, pneumonia attacking every age, and its disposition increasing with increasing age, whereas meningococcic meningitis is an affection of childhood and youth, and beyond thirty-five there is slight disposition to it; pneumonia has a typical course and crisis, while the course of epidemic cerebro-spinal meningitis is irregular and a crisis occurs only rarely; also the complications are different. To this it may be added that the causative organisms differ widely; the one is extra-cellular, the other inter-cellular; the one has a capsule, the other apparently has none, or, at all events, no capsule has been demonstrated up to the present time; the first is oval or conical, the second is biscuit-shaped; the for-

mer is not decolorized by Gram's method, the latter is decolorized by Gram. And they further differ in their cultural properties. Still this difference in biological characteristics would probably not prevent a correlation and interaction between them as yet neither understood nor absolutely determined. Epidemic meningococci meningitis may be complicated by croupous pneumonia (Elsner, Councilman), or may have a meningococci pneumonia for its complication (Councilman). Hun¹⁹ cites a case illustrating the supposed relation between epidemic cerebro-spinal meningitis and pneumonia. Councilman found croupous pneumonia in two of his 111 cases. In the Gouverneur series of 105 cases, croupous pneumonia was present in two instances.

Period of Incubation: Bolduan and Goodwin tabulate 34 instances. from as many houses, in which "there was an interval of varying length between the death or removal of the first case and the onset of the disease in the subsequent case or cases." In 14 of these the interval was from one to seven days. They cite an instance (Case 7) which points strongly to the incubation period having been in that case exactly three days. The incubation period is generally conceded to be about three or four days; but it is a matter difficult to determine, for meningococci have been found in the nasal secretion of healthy attendants, who subsequently have not developed the disease;

and it is conceivable that in those who do develop epidemic cerebro-spinal meningitis, a variable length of time may be taken in the passage of the meningococci from the nasal mucous membrane to the meninges, if it does occur in this way, which appears probable.

BACTERIOLOGY.

Description of the Meningococcus: The meningococcus is the causative factor in a large proportion of the cases of epidemic cerebro-spinal meningitis. It was described by Weichselbaum in 1887, confirmed by Jaeger in 1895, and since then by numerous investigators. Goodwin and Von Sholly,²⁰ in an article in the Chicago Journal of Infectious Diseases, in February, 1906, gives Weichselbaum's findings, and characteristics deemed essential by Albrecht and Ghon in 1901 and 1903. Councilman gives an excellent description of it in the Massachusetts Board of Health Report for 1897. He says when grown in pure culture, "it is a micrococcus of about the same size as the ordinary pathogenic micrococci, and appears in diplococcus form as two hemispheres separated by an unstained interval." They are gonococcus-like in form, and mostly intracellular within the polymorphonuclear cells of the exudate, and often one cell contains a number of diplococci. They take the ordinary stains and are Gram negative. The colonies require frequent transplanting to keep alive, and must be kept at a temperature of from 25 to 42 degrees Cen-

tigrade. "The colonies on agar plates are luxuriant, quite viscid, glistening, gray in direct light, and grayish white in transmitted light. The growth is confined almost entirely to the surface in a stab culture. A pellicle develops on a broth-culture (when the broth is neutral and the cultures are undisturbed for several days). Meningococcus cultures have slight pathogenicity for ordinary animals; and are non-resistant. They grow best on Loeffler's blood-serum, or an agar containing ascitic fluid.

Occurrence in the Body: Meningococci have been found in the nasal mucus of patients with epidemic cerebro-spinal meningitis by a moderate number of investigators. Goodwin and Von Sholly, in the recent epidemic in New York, isolated meningococci in 12 of 22 cases examined during the first week, and in five of 15 examined during the second week; while in a case examined on the sixty-seventh day they found a few colonies. Meningococci have also been isolated from the nares of healthy persons in contact with meningitis patients. These same bacteriologists obtained meningococcus cultures from the nares of over 10 per cent. of these healthy contacts, and from two probable non-contacts a diplococcus was obtained which differed from the meningococcus only in some agglutinating characteristics. Park²¹ says "the complete identity in agglutination characteristics between organisms obtained from the nasal cavity of the sick

and from the spinal fluid is strong proof of the former being not only meningococci but the same identical variety as that found in the cord."

Elsner succeeded in isolating the meningococcus from the blood at some time or other in the course of the disease in 10 out of 41 cases. The organism has, in addition, been isolated from the pus from joints, herpes, pneumonic areas in the lungs, and the conjunctivae of meningitis patients (Netter).²²

In innumerable instances it has been detected in the spinal fluid obtained by lumbar tapping; in fact it appears to be generally present here. It was isolated from the spinal fluid in 76 per cent. of the Gouverneur cases.

DIAGNOSIS.

The diagnosis may be (1) Symptomatic,
(2) Special,
(3) Pathological, or
(4) Differential;

or a combination of two or more of these. I shall not attempt to divide the disease into types, as such a classification appears somewhat arbitrary in view of the fact that epidemic cerebro-spinal meningitis is so irregular in its course, and there being so many gradations in its severity. Then again we cannot generally label a case as of a particular type until the disease

has run its course, and it does not help us from a diagnostic standpoint.

During an epidemic one is on the lookout for the disease, and consequently it is not likely to be overlooked. The sporadic cases present greater difficulty. In general it should be remembered that the affection most commonly attacks people in good health. In Billing's figures of 365 cases, 346 were in apparent good health when stricken.

The onset is almost invariably abrupt, and soon followed by a violent discharge of nervous symptoms. There is not usually a chill. When it is borne in mind that the meninges of the brain and cord, and adjacent nervous substance, and nerve roots are involved, and often covered with a layer or accumulations of purulent exudate, it is not surprising that such a great variability and intensity occur in the symptoms of nervous irritation and paralysis.

1. *Symptomatic Diagnosis:* The mode of onset was sudden in the majority of the Gouverneur cases, that is, in addition to the violent headache and vomiting, and generally fever, pronounced nervous symptoms such as extreme restlessness and irritability, or delirium or coma, or cervical opisthotonus, have manifested themselves within twenty-four hours. In a smaller proportion of the cases the onset was more gradual, perhaps only headache being complained of during the first twenty-four hours, or headache and

vomiting, or headache, vomiting and fever—pronounced nervous manifestations not occurring until the second day or later. A chill occurs only rarely as a prodromal symptom.

The symptoms may be divided into :

- (a) Nervous,
- (b) Constitutional,
- (c) Pertaining to the cutaneous, respiratory, digestive and urinary systems, and joints.
- (d) Special Senses, such as the eye, ear, etc.

(a) *Nervous Symptoms :*

Headache was present in 90 per cent. of the patients over three years of age on the Gouverneur series. It was the first symptom in three quarters of these cases. It generally appeared suddenly, and was, as a rule, intense and severe, “a splitting headache,” remittent, with exacerbations. The patients would sometimes moan, sometimes shriek with the pain. One child compressed his head between his hands, and while screaming would beat the bed and wall with his fists in his endeavor to obtain relief. In a majority it was an occipital headache, in the others, general, or frontal. Billings ascertained that headache was present in 238 of his 365 collected cases. *Vomiting* occurred in 86 per cent. of the Gouverneur patients, and nausea but no vomiting, in two per cent.

It was the first symptom only occasionally. It bore no constant relation to the ingestion of food. In a few patients it was synchronous with the headache; but generally followed the headache by a few hours to a day or more. It was generally not persistent nor exhausting in character. In only a small number did it continue during the course of the disease. In Billings' series 336 patients suffered from it.

Motor Symptoms: This same author gives *convulsions* as having occurred in 245 of those afflicted. A history of general convulsions were obtained in over one-third of the Gouverneur series. They were the primary symptom in only three cases, occurring generally during the progress of the malady, and the younger the child apparently the greater the susceptibility. *Spasmodic contractions* of various groups of muscles, and a muscular tremor were moderately common. *Rigidity* of the post-cervical muscles was elicited in 95 per cent. of the Gouverneur patients; while cervical opisthotonus (in some instances so extreme that deglutition was rendered difficult) was a very common symptom. Billings' figures give retraction of the head as the most common symptom (349 cases out of 365). General opisthotonus rarely occur. A spastic condition of various groups of muscle was tolerably common at Gouverneur, sometimes affecting one or more extremities, sometimes just the flexors of the thumb and fingers. In fact a characteristic *attitude*

is for the patient to lie on one side, with the head retracted, the forearms flexed, the fingers flexed into the palms, and the thighs flexed upon the abdomen and the legs upon the thighs.

Paralysis: Paralysis is not infrequent. Davis²³ mentions particularly paralysis, partial or complete, of the 3rd, 4th, 1st division of the 5th, 6th and 7th nerves. In the Gouverneur series a right sided hemiplegia occurred, a unilateral facial palsy, a lower extremity, both lower extremities, and an arm and a leg on the same side. Motor aphasia occurred in one instance. The *tendon reflexes* are variable; occasionally absent, occasionally present, occasionally absent on one side yet present on the other. Koplik²⁴ found the Babinski reflex present in only 4 out of 25 cases of epidemic cerebro-spinal meningitis, while present in 20 out of 26 cases of tuberculous meningitis. He says: "I regard the presence of this reflex as a valuable addition to the clinical picture of tuberculous meningitis as distinguished from cerebro-spinal meningitis of epidemic type." It does not appear to be valuable, however, in children under two years of age.

Condition of the Sensorium: Pain is a common symptom. The headache has been referred to. An excruciating backache is sometimes complained of, or pain in the abdomen or extremities. Cutaneous hy-

paraesthesia is not often absent at some time or other during the course of the disease. Osler lays stress upon it as one of the most characteristic features of epidemic cerebro-spinal meningitis. Koplik says it is rare in tuberculous meningitis. He found it present in only 3 of 34 cases of this disease. When an attempt is made to overcome the cervical opisthotonus the patient generally evinces pain, but Huber and Monroe²⁵ state that rotation is possible. Pressure is sometimes painful upon the spinous processes, or upon the abdomen or extremities. Patients occasionally shriek with pain upon being touched; extreme irritability and restlessness are not uncommon. Aversion to light and sound will be considered elsewhere. There may be a hydrocephalic cry or grinding of the teeth.

Mental confusion, delirium, apathy or coma are common symptoms. At times it is a low muttering delirium resembling the typhoid status, more often a noisy active delirium. Although delirious at one moment the condition of the sensorium may be peculiarly clear at another, the patient often taking an unusual interest in his surroundings and answering questions in a perfectly rational manner. A relaxation of the sphincters is the rule during these psychical aberrations.

Constitutional Symptoms: *Fever* is present almost invariably; only rarely does the disease run a feb-

rile course. There is nothing especially characteristic about the temperature curve. It is most erratic. The tendency is for it to remain somewhat elevated at first and then to become irregularly remittent or intermittent. In the Gouverneur series it seemed remarkable how at times a clear mental condition obtained in spite of an unusually high temperature, and how occasionally delirium or coma supervened when the curve was practically normal. *The Pulse* usually is of the ordinary febrile type. Uncommonly the pulse-rate is low in proportion to the temperature. Generally the rhythm and force show moderate regularity, unless the patient's condition is assuming unusual gravity. The tension is almost invariably low.

Respiration is considered here as its characteristics are not due to any pathological pulmonary condition. The respiratory rate is generally in proportion to the temperature. The pulse-respiratory ratio is not commonly altered to any significant degree. The type of respiration is in general normal, but it may be irregular or irregular and spasmodic, or typical Cheyne-Stokes' breathing may supervene. These are apparently not common, however.

(c) *Various Symptoms:*

I shall not refer to complications unless of diagnostic value. In the *cutaneous system herpes* is common

in epidemic cerebro-spinal meningitis; it is generally upon the lips or alae of the nose. Huber and Monroe observed it in 16 of 60 cases. Its presence appears to vary in different epidemics. I observed it in 25 of the Gouverneur series of 105 cases. *Petechiæ* appears to be about as common as herpes. Huber noticed petechiæ in 14 of 60 cases. In Billings' figures they are over twice as common as herpes. In the Gouverneur cases the petechiæ appeared earlier in the disease than the herpes. They are said to occur most frequently on the extensor surfaces, the lower part of the abdomen and about the joints. Erythema, urticaria and a roseolous eruption have been noticed. Tache cerebrale may sometimes be produced. Sometimes subcutaneous hemorrhage occurs.

In the *digestive system* constipation is common.

Respiratory system: A coexisting rhinitis and pulmonary congestion and collapse are not uncommon. Less frequent are bronchitis, lobar- and bronco-pneumonia.

In the *urinary system* renal congestion occurred in about one-quarter of the Gouverneur cases.

Other symptoms: The face is often pale; the abdomen is quite frequently retracted; the spleen is rarely palpable. Rapid emaciation occurs. Complications of a septic nature do not apparently often occur.

The Joints: Complications in and about the joints appear to have been far more common in the older epidemics than in the recent ones. North, in 1811, referred to them. Councilman found joint complications in only six of his 111 cases. Osler²⁶ has written a monograph on "The Arthritis of Cerebro-spinal Fever." The knee and elbow are said to be the joints most frequently involved. It may be a peri-articular or truly articular inflammation, and meningococci have been found in some of those cases that have gone on to suppuration.

(d) *Special Senses:* *The eye.* The coexisting eye conditions are important from a standpoint of diagnosis. Huber and Monroe found conjunctivitis present in over 60 per cent. of their cases. Leszynsky²⁷ says that eye symptoms were present in over half of his patients. Randolph, in the Lonaconing epidemic in Maryland, ascertained that 80 per cent. of the cases showed some intraocular change, generally a congestion of the retinal veins and optic disks, and not rarely optic atrophy. Photophobia, diplopia, triptopia, strabismus, are all common. Blindness sometimes supervenes. Some pupillary deviation from the normal is commonly present; the pupils may be equally contracted or equally dilated, sluggish in reacting to light, or not reacting at all. In only four of the Gou-verneur series was marked irregularity observed. An ophthalmoscopic examination may reveal a congested

optic disk, which is apparently present in a large percentage of the cases, or optic neuritis, or neuro-retinitis. Davis states that so marked a swelling of the optic nerve as to give rise to "choked disk" is rarely seen in epidemic cerebro-spinal meningitis, being more commonly met with in tuberculous meningitis, and most often in brain abscess and tumors of the brain. Keratitis, iritis, choroiditis, are apparently uncommon. Panophthalmitis is rare. Leszynsky observed bilateral exophthalmus several times.

The Ear: The ear complications do not appear so frequently as the ocular ones, but are important. An aversion to sound is common, or tinnitus aurium, impairment of hearing, or unbearable pain may occur. Deafness is common. Otitis media and otitis interna are not rare. Mastoiditis has been reported. A staggering gait during convalescence is occasionally manifested. There were ear complications in 16 of Councilman's Boston cases, five being cases of middle-ear disease.

2. *Special Diagnosis:*

Kernig's sign is considered a valuable special diagnostic sign. With the thigh flexed at an angle of 90 degrees upon the abdomen there is opposition, more or less intense, preventing the complete extension of the leg upon the thigh. The manipulations generally produce evidence of pain and sometimes a tremor.

In Billings' series Kernig's sign was stated to be absent in only seven of 365 cases. It was demonstrated in 87 per cent. of the Gouverneur cases. Although almost constantly present in epidemic cerebro-spinal meningitis, it may be present in other pathological cerebral conditions and in diseases with cerebral manifestations. Thus, Koplik says it is more constant in epidemic cerebro-spinal meningitis than in tuberculous meningitis, and may be present in typhoid or pneumonia with cerebral symptoms. Elsner also agrees that it is present in some cases of pneumonia. Leszynsky offers the hypothesis that the resistance to extension is to avoid painful stretching of the sciatic nerve or spinal roots involved in the inflammatory process, and has detected tenderness over the sciatic foramen and along the course of the nerve.

(3) *Pathological Diagnosis:*

Spinal Fluid: Lumbar puncture is by far the most important means of establishing a positive diagnosis. The subarachnoid spaces of the brain and cord are in direct communication, and the cord is small in proportion to the size of the spinal canal, and consequently the latter may contain a large quantity of the inflammatory exudate, especially when it is considered that the inflammatory process is not only cerebral but spinal as well. The average amount from 168 tappings in the Gouverneur series was nearly six

drachms, and as much as eighteen drachms were obtained in one instance. In this spinal fluid obtained by lumbar puncture the causative meningococcus is demonstrable in about three-quarters of the cases. The procedure is perfectly harmless, not difficult to perform, and ought to be resorted to as a routine measure in all suspected cases of infective cerebral or cerebro-spinal trouble.

Concerning the technique of lumbar puncture, I would refer the reader to Dr. Wentworth's²⁸ notes on spinal puncture in the Massachusetts Board of Health Report for 1898, or to Jacoby's²⁹ article in the New York Medical Journal for December 28, 1895, and January 4, 1896.

A dry tap is rare. The fluid obtained in a case of epidemic cerebro-spinal meningitis is turbid in a large proportion of the cases, varying from a thick pus to a slight opalescence; occasionally it is clear, and only rarely hemorrhagic. In most cases it comes out under pressure, in spurts, influenced by respiration and by crying. A sediment is generally deposited in the test-tube within a few hours; in a few cases a delicate central skein forms. Smears of the sediment should be made upon two slides and fixed by heat. One should be stained by one of the ordinary stains, such as anilin-gentian-violet and examined. If a gonococcus-shaped diplococcus is seen within the polymorphonuclear cells, the second slide should be sub-

jected to Gram's method of staining, decolorizing and counterstaining. The meningococcus is negative to Gram. Now, if a Gram-negative, biscuit-shaped, intracellular diplococcus is found in the spinal fluid it is in all probability the meningococcus. The gonococcus and the micrococcus catarrhalis might fulfill these conditions, but such a possibility is extremely minute. But in order to be absolutely certain of the organism being the meningococcus, cultural and agglutinating tests have to be employed. Kalberlah³⁰ says that in making cultures it is well to allow the spinal fluid to flow directly into Loeffler's blood-serum, to protect from cooling while in transit to the incubator, and to make a microscopical examination from the fresh specimen and after from 12 to 24 hours' cultivation. Gouverneur Hospital was fortunate in the period mentioned by having Bolduan and Goodwin, of the New York Board of Health Research Laboratory conduct these tests in return for the material furnished. Some authors have called attention from a diagnostic standpoint to the microscopical appearance of the spinal exudate in infective cerebral diseases, and upon the amount of albumin and other ingredients present. This subject needs further study.

Meningococci are generally quite plentiful in the spinal exudate in cases of epidemic cerebro-spinal meningitis, but occasionally the fluid requires to be centrifugalized and a great deal of patience expended before the organism is found. A negative result does

not justify any conclusions. A sterile test-tube must be used, and contamination by means of extraneous organisms prevented. The consensus of opinion seems to be that there is a mononuclear leucocytic increase in the spinal fluid of tuberculous meningitis.

The Blood: A polymorphonuclear leucocytosis is the rule in cerebro-spinal fever, ranging from 10,000 per cubic millimetre to 40,000, or even more. Osler was of the opinion that a leucocytosis had no especial value in the differential diagnosis of the various forms of meningitis. Elsner mentions the absence of it, however, as a diagnostic point in favor of typhoid with cerebral symptoms. Neither the red blood cells nor the hæmoglobin show any marked reduction. At present they cannot be said to possess diagnostic value. Meningococci have been isolated from the blood by several observers. They do not appear to be constantly present, nor ever in sufficiently large numbers. This procedure, from a diagnostic standpoint, cannot be compared to the facility with which meningococci may be demonstrated in the spinal fluid.

Isolation from the Nose, Conjunctivæ, Herpes, etc.: Isolation from the nasal secretion of a patient with cerebro-spinal symptoms is very suggestive, but cannot be regarded as positive evidence of epidemic cerebro-spinal meningitis, for the nasal cavity is physiologically on the outside of the body. And the same may

be said of the isolation from the conjunctival secretion. Cultural and other tests are necessary to establish identity in these cases owing to the presence of the micrococcus catarrhalis and other organisms. Isolation from herpes and from the joints: These conditions are far from constant; and even when present the meningococcus has only occasionally been isolated from them. This procedure as a diagnostic measure is open to apparent objections.

Agglutination Tests: The sera of meningitis patients and of animals immunized for a long time with meningococci have been found to agglutinate meningococcus cultures in low dilutions. Goodwin and Von Sholly used the serum of a sheep which had been inoculated for three months with meningococci and then tried its agglutinating powers upon 21 cultures taken from the nares of meningitis patients and 21 cultures from the spinal fluid. Of the 42 cultures, 41 were agglutinated more or less completely by a 1:20 dilution, 37 cultures were agglutinated by a 1:50 dilution, 30 by a 1:100 dilution, etc. This work is still in an experimental stage, but it is within the realm of probability that this agglutinating test may later prove of some diagnostic import, for in the few instances of epidemic meningococci meningitis where the spinal fluid fails microscopically and by culture to reveal the meningococcus, such a positive reaction might be of value in establishing the diagnosis, and conversely, in

a cerebral disease caused by some other organism a negative reaction would be of value in excluding meningococci meningitis.

4. *Differential Diagnosis:*

The principal diseases which might be confused with epidemic cerebro-spinal meningitis are:

(a) Primary Infective Cerebral Diseases, such as primary pneumococcic meningitis. (Osler does not consider a primary tuberculous meningitis.)

(b) Infective Cerebral Diseases secondary to some lesion elsewhere, such as (1) tuberculous meningitis, (2) pneumococcus meningitis, (3) suppurative meningitis due to the ordinary pus-organisms, and (4) due to miscellaneous organisms such as the typhoid, influenza, diphtheria, and anthrax bacilli; to the gonococcus, etc.

(c) Diseases with cerebral symptoms, but with no actual lesion of the cerebro-spinal axis, such as typhoid, pneumonia, typhus, malignant smallpox, influenza, septicæmia, and toxæmia.

(d) Non-infective cerebral diseases, such as apoplexy, alcoholic cerebral cedema, etc.

The sporadic cases of meningococci meningitis will prove more difficult than the epidemic ones. The points in favor of meningococci meningitis are the sudden onset, the violent and rapid involvement of the

entire cerebro-spinal axis, the cutaneous hyperæsthesia, the remarkable mental clearness and interest displayed in the surroundings; the frequency of herpes, petechiæ, nasal discharge and conjunctivitis; the varying course and relapses; and the selection of the eyes, ears and joints for complications. Finding the meningococcus in the nasal secretion renders the diagnosis probable; and isolating it from the spinal fluid positively decides it. As a routine procedure in all cases with marked cerebral symptoms a lumbar puncture should be made, the fluid centrifugalized and the sediment examined microscopically, and, where possible, subjected to cultural, animal, and agglutinating experiments.

(a) Osler considers primary pneumococcic meningitis as of a rare occurrence in this country; the clinical differences from meningococcic meningitis have not yet been clearly established, and, at the present time, we must rely mainly upon lumbar punctures to settle the diagnosis.

(b) 1. In tuberculous meningitis the primary focus may sometimes be discovered; there is a prodromal period and longer onset; the cerebral, especially the basilar, symptoms predominate over the spinal; there is not always a leucocytosis; the mononuclear cells are said to be increased in the spinal fluid; the Babinski reflex is more common (Koplik); coma and

drowsiness appear to be more constant; there are generally no cutaneous nor joint symptoms; the pulse often manifests irregularity, and choroidal tubercles may be discovered by the ophthalmoscope. Owing to the difficulty in isolating the tubercle bacillus from the spinal fluid, a sterile tap argues in favor of tuberculous meningitis and against meningococcic. Inoculations into guinea pigs may have to be resorted to in order to demonstrate the presence of the tubercle bacillus in the spinal fluid.

2. In secondary pneumococcic meningitis the pulmonary lesion may be detected or a history of trauma obtained; it occurs generally in older patients; spinal symptoms are uncommon; the cerebral symptoms are not apt to be severe; the sensorium is duller; it is rapidly fatal. Lumbar puncture is essential. It must be remembered that meningococcic meningitis may be complicated by a meningococcic pneumonia, and that a croupous pneumonia may be complicated by a meningococcic meningitis.

3. Secondary pyogenic meningitis: The history is important. A history of trauma to the skull; a primary lesion elsewhere, such as erysipelas of the face and scalp, disease of the ear, nose or sinuses; ulcerative endocarditis, etc. The cerebral symptoms are marked and the spinal less common. Blood cultures and lumbar punctures are sometimes necessary for diagnosis.

(c) 1. In typhoid with cerebral symptoms, the slower onset, epistaxis, characteristic temperature curve, the apathy, the enlarged spleen, intestinal symptoms, and the special tests such as the Widal reaction. There is generally no actual leucocytosis in typhoid; and lumbar tap is negative.

2. Pneumonia with cerebral symptoms: The usual history of a prodromal chill; the lesion in the lungs, the altered pulse-respiratory ratio, the maintained temperature, the crisis with a sudden disappearance of the cerebral symptoms, and negative lumbar puncture.

3. Typhus with cerebral symptoms: The less sudden onset; the characteristic rise of the fever, and the maintenance, the slower appearance of the meningeal symptoms. Kernig's sign is generally absent. The less frequent occurrence of photophobia, aversion to sound, ocular and facial palsies, and cervical retraction. True typhus may be complicated by meningitis (Omerod).³¹ Negative lumbar puncture.

(d) The non-infective cerebral diseases: Apoplexy, traumatic cerebral hemorrhage, and alcoholic cerebral oedema will only very rarely be confused with meningococcic meningitis.

After the differential points have been carefully weighed, I cannot urge too strongly the importance of the lumbar puncture in those cases in which any doubt remains, the simplicity of the technique, and the harmlessness of it when ordinary aseptic precautions are taken.

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